OPEM

Oriental Pharmacy and Experimental Medicine 2003 **3(4)**, 163-179 **Review**

Functional bioactivity of *Polygonatum* species

Noboru Motohashi[1,*], Guo-Wen Zhang[2] and Yoshiaki Shirataki[3]

[1]*Meiji Pharmaceutical University, Kiyose-shi, Tokyo, Japan;* [2]*Institute of Botany, Academia Sinica, Laboratory of Phytochemistry, 141, Xi Wai Da Jie, Beijing, China;* [3]*Pharmaceutical Science, Josai University, Sakado-shi, Saitama, Japan*

SUMMARY

The genus Polygonatum species belongs to the family Liliaceae which is widely distributed over areas of the north temperature zone. There are about forty more plants of *Polygonatum* species in the world widely distributed in eastern Europe and south east Asia. The plants of *Polygonatum* species have been used not only as ornamental plants but also for their medicinal values. This article is concerned with the specific properties and flavour of the drug and its history as a medicine, showing the main functional components of *Polygonatum* species of flavonoids, steroidal glycosides, and saccharides.

Key words: *Polygonatum* species; Cardivascular; Blood sugar; Lung and liver; Flavonoids; Saponins; Saccharides

INTRODUCTION

Polygonatum species have been used in the treatments of many diseases as Chinese folklore medicine. Liu explained the preliminary understanding of drug-induced toxic deafness as a side drug effect treated actually with *Polygonatum*, using a clinical remedy analysis of 100 cases (Liu, 1982). How to identify the adulterates of the genus *Polygonatum* in Sichuan as medicinal plants was revealed (Liu, 1985). Sixteen species of medicinal plants of *Polygonatum* in northwest China were refered by their distribution, ecological conditions, infraspecies variations and clinical applications (Ding and Zhao, 1991).

In eastern Europe, Japan and southern Asia, *Polygonatum* species have also been used medicinally. The rhizome of *P. falcatum* A. Gray. is widely used for the purpose of analeptic in southeast Asia (Tomoda and Nakatsuka, 1972), the rhizome of *P. odoratum* var. pluriflorum is used as a tonic in Japan (Sugiyama *et al*., 1984), and *P. polyanthemum* [M.B.] Die is used as a folklore drug in eastern Europe (Rakhmanberdyeva *et al*., 1982a). Because of the historical and current medical uses of *Polygonatum* species, many scientists have begun to pay close attention to *Polygonatum* species. Consequently, the compositions of Rhizomes for *P. cyrtonema* Hua, *P. kingianum Coll* et Hemsl, *P. souliei Hua*, *P. cirrhifolium* (Wall.) Royle, *P. cathcartii* Bak., *P. marmoratum* Levl., *P. resem* (Ledeb.) Kunth, *P. macropodium* Turcz, *P. filipes* Merr., *P. verticillatum* (L.) All. (Delectis Florae Reipublicae Popularis Sinicae Agendae Academiae Sinicae, 1978; Compile group of "Quan Guo Zhong Cao Yao Hui Bian", 1975; Chopin *et al*., 1977), *P. polyanthemum* [M.B.] Die and *P. multiflorum* (L.) All. (*P. cyrtonema* Hua) (Chopin *et al*., 1977), *P. kingianum* Coll. et Hemsl. (Li *et al*., 1992) and *P. prattii* Baker (Li *et al*., 1993) have been investigated. Here, the purpose of this review paper is to potentially search the possibility of their functional properties of a plant therapy on three compounds of flavonoids, saponins, and saccharides which contained mainly the functional components in *Polygonatum* species.

THE PLANTS AS MEDICINE

In around over 5000 years history, *Polygonatum* species have been applied in both Oriental, especially Chinese and European natural folklore remedies.

*Correspondence: Noboru Motohashi, Meiji Pharmaceutical University, 2-522-1 Noshio Kiyose-shi, Tokyo 204-8588 Japan. Tel & Fax: +81-424-95-8953; E-mail: motohasi@my-pharm.ac.jp

Improvement of cardivascular and blood sugar

Rhizomes of *Polygonatum odoratum* (Mill.) Druce var. pluriflorum (Miq.) Ohwi, *Polygonatum macropodium* Turcz., *Polygonatum involucratum* Maxim., and *Polygonatum inflatum* Komar. had the anti-high blood pressure, action of cardiotonic such as cardiac infarction, the reduction of the affection for blood sugar such as diabetes and other diseases (Jiangsu New Medical College, 1977a).

A methanol extract of rhizome of *Polygonatum multiflorum* reversed a normal cardiotonic activity in a rat left atrium, by the increasing of cAMP. The extract also inhibited the phosphodiesterase activity. This means that the cardiotonic activity by the methanol extract might enhance the sympathetic nervous system, which enhancement was produced by rising the level of cAMP. On the other hand, propranolol of a β-adrenoceptor antagonist treated left atrium had a median cardiotonic activity between a control and the methanol extracts, but, phentramine of a α-adrenoceptor antagonist treated left atrium was not changed. From above results, it suggests that the cardiotonic action of methanol extract might indirectly stimulate the β-adrenoceptors (Hirai *et al*., 1997). The methanol extract of rhizomes of *Polygonatum officinale* showed a reduction of the blood glucose of normal mice after 4 hr intraperitoneal (ip) administration and similarly, signifincantly reduced the blood glucose of streptozotocin-induced diabetic mice after same 4 hr ip administration. Very interestingly, the methanolic extracts further inhibited a blood glucose in epinephirine-induced hyperglycemic mice. The extracts, however, increased also the liver glycogen in an epinephirine-induced hyperglycemic mice. This means that the methanol extracts had its hypoglycemic effects by decreasing the hepatic glucose production of epinephirine-induced hyperglycemic mice and then the glucose uptake in liver cells of the mice increased molst visually, because the methanol extracts lowered dramatically the blood glucose levels of streptozotocin-induced diabetic mice (Kato and Miura, 1993; Kato and Miura, 1994). N-Acetylneuraminic acid and several sialyl-glycoproteins inhibited the agglutinating activity of *Polygonatum multiflorum* [L.] All (Antoniuk, 1996). The effects of three steroidal glycosides (SG-100, SG-280, and SG-460) obtained from *Polygonatum odoratum* (Mill.) Druce. were examined on insulin secretion, insulin action, and relative glucose uptake in the various tissues of 90% pancreatectomized male Sprague-Dawley rats. The serum glucose levels were lowest in the rats receiving the SG-100. The insulin secretion from pancreatic β-cells had no change even with each three SG administration. The whole-body glucose disposal rates increased, following each concentration by 39% SG-100 administration. The SG-100 increased both the glycogen contents and glycogen synthase activity in the soleus muscle of pancreatectomized rats. Uptake of [1-(14)C]2-deoxyglucose into the soleus muscle was higher in such rats receiving the SG-100 than in rats receiving other compounds. These results suggest that the SG-100 has an antihyperglycemic effect by promoting the peripheral insulin sensitivity without changing the insulin secretion (Choi and Park, 2002).

On the hypoglycemic effect of rhizomes of *Polygonatum sibricum* and *Polygonatum officinale* using KK-Ay mice, one of the animal models of non-insulin dependent diabetes mellitus (NIDDM) was used. The methanol extract of rhizomes of both *Polygonatum sibricum* (OM) and *Polygonatum officinale* (IM) reduced the blood glucose levels of KK-Ay mice 4 hr after intraperitoneal (ip) administration. On the hypoglycemic effect, the blood glucose of 1 M was lower than that of OM. IM-treated mice significantly decreased the blood glucose level in an insulin tolerance test, but OM-treated mice did not change. It suggests that the hypoglycemic effect of IM raised the insulin sensitivity (Miura and Kato, 1995).

The binding effects of insulin with human erythrocyte insulin receptor were tested for five Chinese herbal drugs, *Trichosauthes kirilowii* (TK), *Polygonatum sibiricum* (PS), *Scrophularia ningpoensis* (SN), *Anemarrhea asphodeloides* (AA). TK, PS, and SN did not increase nor decrease the insulin receptor binding rate, whereas AA provoked a marked inhibiting effect on the rate of binding (P less than 0.01). Five different effects, however, directly do not mean the beneficial effect of five plant extracts on remedy of diabetes, because first, the tests were performed *in vitro* but not *in vivo* and the erythrocytes from normal men but not from the true diabetics., second, each five extract was not

from a Chinese traditional method such as decoctions, and third, the fact that there is no effect on some insulin receptor bindings, which cannot rule out the beneficial effect on other aspects of insulin or the insulin secretion even on the reversal of the tissue insulin resistance and consequently, this test is very far from actual drug application (Liu *et al*., 1991).

Improvement of lung disease

Rhizome of *Polygonatum cirrhifolium* (Wall.) Royle plays a role to enhance the function for moistening the weak and tired lung and nourishing negative heart's world, invigorating the spleen and replenishing the refreshed heart-soul, elimination phlegm and hemostasis, detumescence and removing the toxic materials, and the remedies such as a consumptive disease and dyspneic cough, dizzy, poor appetite, seminal emission, night sweat, metrorrhagia and morbid leukorrhea, debility, hematemesis, bleeding, hematemesis by trauma, throat swelling and painful, sore swelling, scrofula (Jiangsu New Medical College, 1977b).

Rhizome of *Polygonatum ensifolium* Lěvl (*Disporopsis* (Hua) Diels) also showed the function on the improvement of nourishing a negative heart's world and moistening the lung, the production of body fluid and quench one's thirst, and menoxenia (Jiangsu New Medical College, 1977f).

Improvement of liver disease

Rhizomes of *Polygonatum verticillatum* (L.) All and *Polygonatum roseum* (Ledeb.) Kunth were effective for the liver to stop the wing, nourishing a negative heart's world and clear eyes, clearing away the heat and cooling blood, and headache and eye disease, throat pain, high blood pressure, epilepsy and furuncle (Jiangsu New Medical College, 1977c). A complex administration with *Polygonatum sibiricum* improved a chronic hepatitis B (Chen, 1990).

Antimicrobial activity

Rhizome of *Polygonatum punctatum* Royle was effective for carbuncle and furuncle (Jiangsu New Medical College, 1977d). Rhizomes of *Polygonatum sibiricum* Redoute, *Polygonatum cyrtonema* Hua, *Polygonatum macropodium* Turcz., *Polygonatum kingianum* Coll. et Hemsl., *Polygonatum cirrhifolium* (Wall.) Royle, *Polygonatum roseum* (Ledeb.) Kunth, *Polygonatum verticillatum* (L.) All., *Polygonatum curvistylum* Hua, *Polygonatum erythrocarpum* Hua, *Polygonatum filipes* Merr., and *Polygonatum lasianthum* Maxim. were antibiotic, antifugus and antihypertensive (Jiangsu New Medical College, 1977e).

CHEMICAL COMPONENTS OF POLYGONATUM SPECIES

A lot of *Polygonatum* species have been studied to date. The chemical components of *Polygonatum* species have been complicated. Generally, *Polygonatum* species may contain mainly functional flavonoids, saponins, and saccharides. Additionally, some of *Polygonatum* species contain alkaloids (Crum *et al*., 1965; Constantinescu *et al*., 1969), aldehydes (Isono *et al*., 1974), quinones (Constantinescu *et al*., 1969), and steroids also.

Flavonoids

Flavonoids are well known as the plant pigments providing a significant protection against some cancers, heart disease and strokes such as myocardial infarction. The clinically representatives of the flavonoids are quercetin, citrus bioflavonoids and hydroxyethylrutosides. Flavonoids help to act the strong antioxidants in providing the protection against the harmful oxidative and free oxygen radical damages by superoxide radical and hydroxy radical. Generally, flavonoids are usually the vegatable yellow coloring matters with 2-phenylchromone which distributes widely ubiquitous in *Polygonatum* species (Fig. 1). By different skeletons, flavonoids were classified to flavone, flavonol, flavane, flavanone, chalcone and anthracyanidin.

Most well-known flavonoids help to reduce the

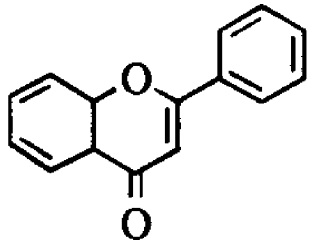
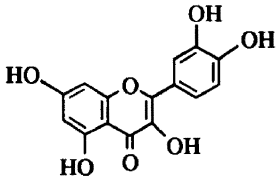
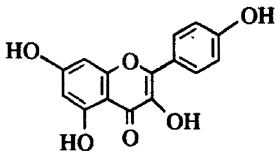
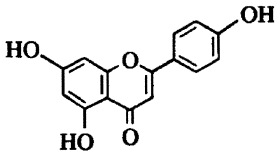
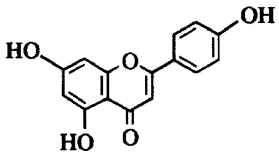
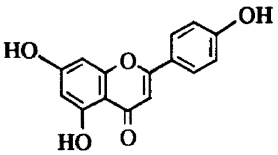
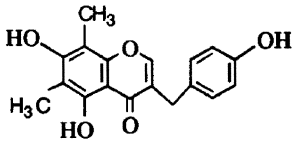
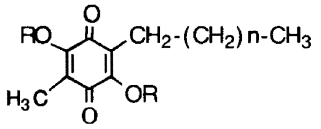
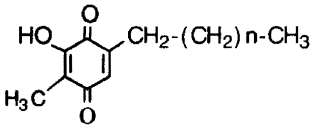


Fig. 1. 2-Phenylchromone.

Table 1. The flavonoids isolated from *Polygonatum* species

species	plant's part	aglycone	sugar	reference
P. polyanthemum [M.B.] Die	stem, leaf	quercetin 	3-O-rutinoside	Akhmedova, 1938
P. officinale All.	stem, leaf	quercetin kaempferol 	3-O-rutinoside glucose, rhamnose	Nakov *et al.*, 1976
P. odoratum (Mill.) Druce var. *pluriflorum* (Mig.) Ohwi	leaf	apigenin 	6-*C*-β-D-glycopyranosyl-7-O-β-D-glucopyranoside; vitexin-2''-O-glucoside; vitexin-2''-O-sophoroside (glucosyl (1-2) glucoside	Morita *et al.*, 1976
P. multiflorum L.,	stem, leaf	apigenin 	5,7,4'-trihydroxyflavone 8-*C*-β-D-glycosylxyloside; 5,4'-dihydroxyflavone 6-*C*-β-D-glycosylrhamnoside.	Skrzypczakowa, 1969
	leaf	apigenin 	8-*C*-β-D-glycopyranosyl-; 6-*C*-hexosyl-8-*C*- pentosyl-; 6-*C*-arabinosyl-8-*C*-hexosyl-.	Chopin *et al.*, 1977
P. alte-lobatum	rhizome	rhizome *C*-methylated homoisoflavanone 		Huang PL *et al.*, 1997
	rhizome	(Two polygonaquinones)   polygonaquinone A: R=H, n=19-21 polygonaquinone B: n=19-21		Huang PL *et al.*, 1997

inflammation, protect the liver, and relieve a cough among other properties. The structure-activity relationship on the inhibition of aldose reductase by flavonoids was found (Kintya *et al*., 1978; Janeczko and Sendra, 1979; Stringina and Isakov, 1982). The flavonoids revealed the strong inhibition against a bovine lens aldose reductase and a broad structure-activity correlation was deduced (Iinuma *et al*., 1989). Because of these activities, the preparations and their medicinal applications for the treatment of human diseases have been investigated (Havsteen, 1983).

Many types of flavonoids have been isolated from *Polygonatum* species. Table 1 shows the flavonoids isolated from *Polygonatum* species (Chopin *et al*., 1977; Akhmedova, 1979; Nakov *et al*., 1976; Morita *et al*., 1976; Skrzypczakowa, 1969). Rhizomes of *Polygonatum alte-lobatum* contains two 1,4-benzoquinones of polygonaquinone A and B, and a novel C-methylated homoisoflavanone and gentrogenin glycoside (Huang *et al*., 1997).

Saponins

Saponin is a glycoside of triterpene or steroid which distributes usually in plant. In details, saponins are one of steroidal or triterpenoid amphiphilic glycosides with surface-active and emulsion-stabilizing properties. The levels of saponins help to maintain in fat-containing plant foods and oils. The saponins could not be absorbed under a normal circumstances. The saponins in body, however, is very important for a possibility of cholesterol precipitation and the interference with micelle formation in the small intestine by enhancing the binding of bile acids with a dietary fiber (Oakenfull and Fenwick, 1978; Oakenfull and Topping, 1983; Topping *et al*., 1980). Saponins help to increase a biliary cholesterol saturation (Nervi *et al*., 1989).

The saponins isolated from *Polygonatum* species are the glycosides of steroids in the structure. Saponin also is generally known to have hemolysis and ichthytoxin actions. The direct administration of saponins is rarely for the clinical treatments. However, diosgenin is a steroidal saponin and the contraception of diosgenin is widely used worldwide. The steroidal saponins have been found in *Polygonatum* species (Table 2) (Kerimov and Nasudari, 1971; Okanishi *et al*., 1975; Kintya *et al*., 1976; Janeczko and Sendra, 1979; Janeczko, 1980; Strigina and Isakov, 1980; Sendra and Janeczko, 1981; Janeczko and Sibiga, 1982; Sugiyama *et al*., 1984; Glebko *et al*., 1986; Janeczko *et al*., 1987; Yesilada, 1987; Glebko *et al*., 1988; Son *et al*., 1990). *P. verticillatum* (L.) All contains about 2.2% diosgenin. Therefore, *P. verticillatum* (L.) All could be a very good source of diosgenin for the pharmaceutical industry.

Two steroidal saponins in the fresh rhizomes in *Polygonatum orientale* were found. One of two is PO-1, sceptrumgenin-3-O-β-lycotetraoside or 3-O-β-Dxylopyranosyl(1(*r*)3)[β-D-glucopyranosyl(1(*r*)2)] β-D-glucopyranosyl(1(*r*)4)-β-D-galactopyranosyl-spirost-5(6),25(27)-dien-3β-ol and other is PO-2, sceptrumgenin-3-O-β-glucopyranosyl(1(*r*)3)[β-D-glucopyranosyl(1(*r*)2)] β-D-glucopyranosyl(1(*r*)4)-β-D-galactopyranosyl-12-oxo-spirost-5(6), 25(27)-dien-3β-ol (Table 2 (cont. 3)) (Yesilada and Houghton, 1991).

Three steroidal glycosides of paratiosides A, B and C, and three prosapogenins of pratiosides D_1, E_1 and F_1 were determined from roots of *Polygonatum prattii* (Table 2 (cont. 3)) (Li *et al*., 1993) . The structures of paratiosides A, B and C, and three prosapogenins of pratiosides D_1, E_1 and F_1 were pratioside A for pennogenin-3-O-β-D-glucopyranosyl-(1(*r*)2)-β-D-glucopyranosyl(1(*r*)4)-β-D-galactopyranoside, pratioside B for 26-O-β-D-glucopyranosyl-22-hydroxy-(25*R*)-furost-5-en-3β,17α,26-triol 3-O-β-D-glucopyranosyl-(1(*r*)2)-β-D-glucopyranosyl(1(*r*)4)-β-D-galactopyranoside, pratioside C for 27-O-β-D-glucopyranosyl-isonarthogenin-3-O-β-D-glucopyranosyl(1(*r*)2)-β-D-glucopyranosyl (1(*r*)4)-β-D-galactopyranoside, pratioside D_1 for gentrogenin-3-O-β-D-glucopyranosyl(1(*r*)2)-β-D-glucopyranosyl(1(*r*)4)-β-D-galactopyranoside, pratioside E1 for isochiapagenin analog, and pratioside F_1 for 25(*R*)-spirost-5en-3β,12α,17α-triol-3-O-β-D-glucopyranosyl(1(*r*) 2)-β-D-glucopyranosyl(1(*r*)4) β-D-galactopyranoside, respectively (Table 2 (cont. 3)) (Li *et al*., 1993).

A steroidal saponin, POD-II, from the ethanol extract of rhizomes of *Polygonatum odoratum* was found as 3-O-β-D-glucopyranosyl-(1(*r*)2)-[β-D-xylopyranosyl-(1(*r*)3)]-β-D-glucopyranosyl-(1(*r*)4)-galactopyranosyl-25(*R*)-spirost-5-en-3β,14α-diol. The POD-II induced the colony stimulating factor (CSF) in a mouse serum. The analog POD-III was synergic

Table 2. Steroidal saponins isolated from Polygonatum species

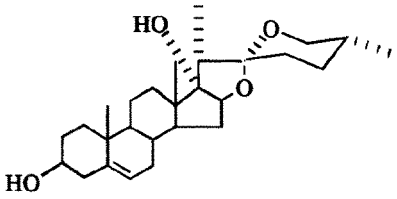
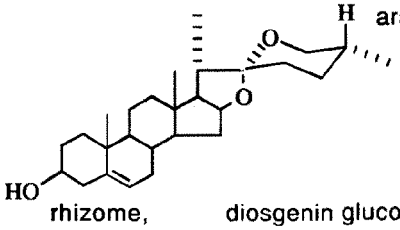
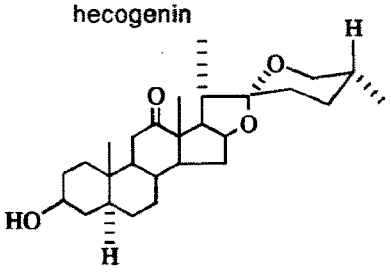
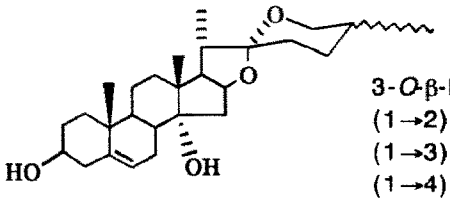
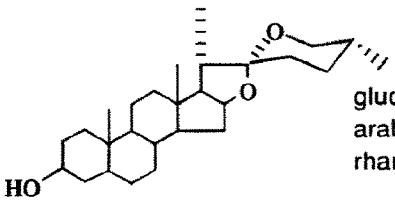
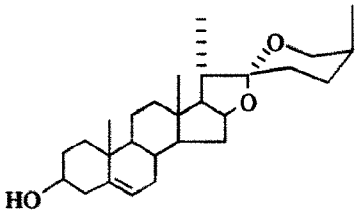
species	plant's part	steroidal aglycone	sugar	reference
P. stenophyllum Maxim.	rhizome	pennogenin 	rhamnose, glucose	Strigina *et al.*, 1980
	rhizome	pennogenin	rhamnose, arabinose, glucose	Strigina *et al.*, 1982
	root,rhizome	pennogenin		Glebko *et al.*, 1986
P. acuminatifolium Kom.		pennogenin		Glebko *et al.*, 1988
P. desoulavyi Kom.	rhizome	pennogenin		Glebko *et al.*, 1988
P. humile Fisch. ex Maxim.		pennogenin		Glebko *et al.*, 1988
P. inflatum Kom.	stem	pennogenin		Glebko *et al.*, 1988
P. involucratum (Franch. et Savat.) Maxim.		pennogenin		Glebko et al., 1988
P. maximowiczi Fr. Schmidt	leaf	pennogenin		Glebko *et al.*, 1988
P. odoratum (Mill.) Druce		pennogenin		Glebko *et al.*, 1988
P. latifolium [Jacq.] Desf.	rhizome	diosgenin 	glucose, galactose, xylose, arabinose	Kintya *et al.*, 1976
P. multiflorum [L.] All.	rhizome, stem, leaf	diosgenin	glucose, galactose, xylose	Janeczko, 1980 Janeczko *et al.*, 1979
	root,rhizome, serial parts	diosgenin		Sendra *et al.*, 1981
P. officinale All.	rhizome	diosgenin		Okanishi *et al.*, 1975
P. verticillatum [L.] All.	rhizome	diosgenin		Yesilada, 1987
	rhizome	diosgenin		Janeczko *et al.*, 1982
P. acuminatifolium Kom.		diosgenin		Glebko *et al.*, 1988
P. desoulavyi Kom.	rhizome	diosgenin		Glebko *et al.*, 1988
P. humile Fisch. ex Maxim.		diosgenin		Glebko *et al.*, 1988
P. latifolium [Jacq.] Desf.	stem	diosgenin		Glebko *et al.*, 1988
P. involucratum (Franch. et Savat.) Maxim.		diosgenin		Glebko *et al.*, 1988
P. maximowiczi Fr. Schmidt	leaf	diosgenin		Glebko *et al.*, 1988
P. odoratum (Mill.) Druce		diosgenin		Glebko *et al.*, 1988

Table 2 (cont 1). Steroidal saponins isolated from *Polygonatum* species

species	plant's part	aglycone	sugar	reference
P. falcatum A. Gray	rhizome	hecogenin 		Okanishi *et al.*,1975
		25*R and S*-spirost-5-en-3β,14α-diol 	3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-(PO-2)	Kato *et al.*, 1993
P. polyanthemum [M.B.] Die	rhizome	smilagenin 	glucose arabinose rhamnose	Kerimov *et al.*,1971
P. sibiricum Redoute	rhizome	yamogenin 	3-O-β-lycotetraoside	Son *et al.*, 1990

for the suboptical and optical concentration of concanavalin A (Con A) and lipopolysaccharide (LPS) to stimulate the lymphocytes proliferation (Lin *et al.*, 1994).

Dioscin, a saponin from the root of *Polygonatum Zanlanscianense* Pamp, significantly inhibited the proliferation of Hela cells. This means that Hela cells underwent the apoptosis in the dose- and time-dependent manners when Hela cells was treated with Dioscin. At the same time, caspase-3, -8 and -9 activities were also detected. Consequently, the low enzymatic activity of caspase-8 and high

Table 2 (cont 2). Steroidal saponins isolated from *Polygonatum* species

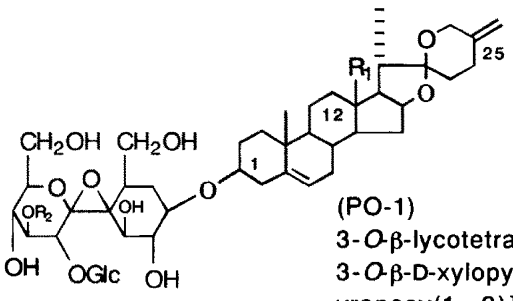
species	plant's part	aglycone	sugar	reference
P. odoratum var.*pluriflorum*		yamogenin	2-β-lycotetraoside	Sugiyama *et al.*, 1984
P. odoratum var.*pluriflorum*	rhizome	neoprazerigenin A		Sugiyama *et al.*, 1984
	rhizome	25*R*-spirost-5-en-3β,14α-diol	3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-galactopyranosyl-	Lin *et al.*, 1994
P. sibiricum Redoute	rhizome	neoprazerigenin A		Son *et al.*, 1990
P. officinale All.	rhizome	25*R*-spirost-5-en-3β,14α-diol	3-*O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-(odospiroside)	Janeczko *et al.*, 1987
	rhizome	25*R*-furost-5-en-3,22,26-triol	3-*O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranosyl-(polyfuroside)	Janeczko *et al.*, 1987

activity of caspase-9 means that the mitochondrial pathway was activated in apoptosis by dioscin. The reduced expression of the survival protein Bcl-2 also confirmed this result. These results will contribute to find a new drug for treatment of human cervical cancer (Cai *et al.*, 2002).

Two saponins, methyl protodioscin and dioscin, were found from the root of *Polygonatum*

Table 2 (cont 3). Steroidal saponins isolated from *Polygonatum* species

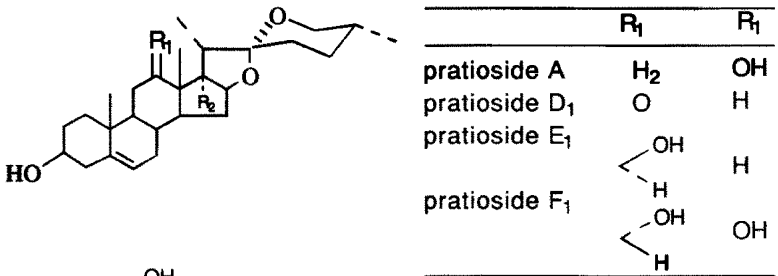
species	plant's part	aglycone	sugar	reference
P. orientale	rhizome	sceptrumgenin (PO-1) akyrogenin (PO-2)		Yesilada E *et al.*,1991



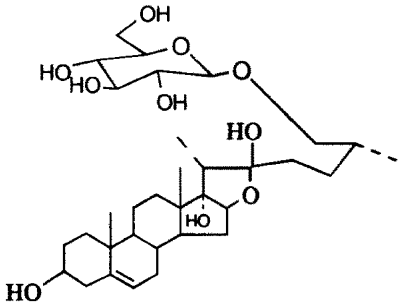
	R_1	R_1
PO-1	H	Xyl
PO-2	=O	Glc

(PO-1)
3-*O*-β-lycotetraoside or
3-*O*-β-D-xylopyranosyl(1→3)[β-D-[β-D-glucopyranosy(1→2)] β-D-glucopyranosyl(1→4) β-D-galactopyranosyl-spirost-5(6), 25(27)-dien-3β-ol
(PO-2)
3-*O*-β-D-glucopyranosyl-(1→3)-[β-D-glucopyranosyl-(1→2)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-12-oxo-spirost-5(6),25(27)-dien-3β-ol

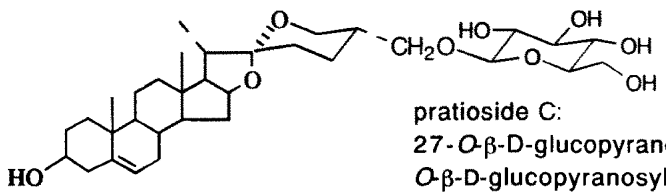
P. prattii	roots	pratioside A, p. B, p. C, D_1, p. E_1, p. F_1	Li X-C *et al.*, 1993



	R_1	R_1
pratioside A	H_2	OH
pratioside D_1	O	H
pratioside E_1		H
pratioside F_1		OH



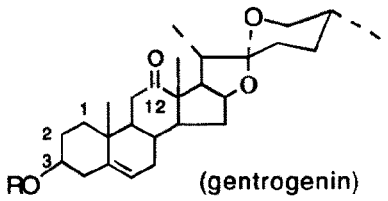
pratioside B:
26-*O*-β-D-glucopyranosyl-22-hydroxy-(25R)-furost-5-en-3β,17α,26-triol
3-*O*-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl(1→4) β-D-galactopyranoside



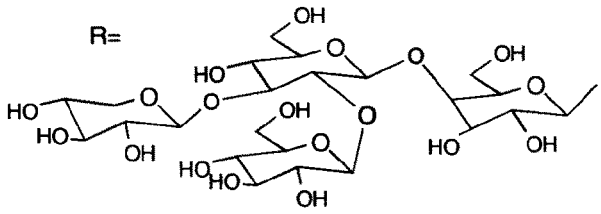
pratioside C:
27-*O*-β-D-glucopyranosyl-isonarthogenin-3-*O*-β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl(1→4) β-D-galactopyranoside

Table 2 (cont 4). Steroidal saponins isolated from *Polygonatum* species

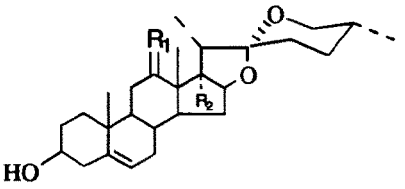
species	plant's part	aglycone	sugar	reference
P. alte-lobatum	rhizome	gentrogenin glycoside		Huang PL *et al.*, 1997



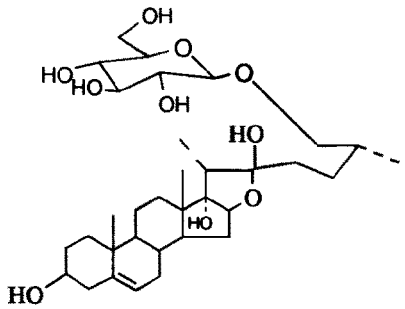
(gentrogenin)
3-*O*-β-D-glucopyranosyl(1→2)-[
β-D-xylopyranosyl(1→3)]-β-D-glucopyranosy
(1→4)-β-D-galactopyranoside



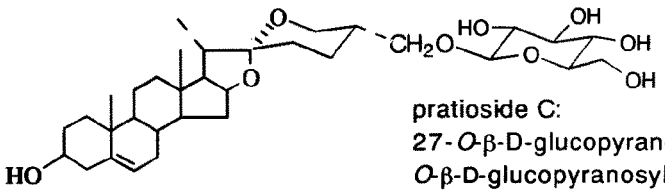
XXXP. prattii	roots	pratioside A, p. B, p. C, D_1, p. E_1, p. F_1		Li X-C *et al.*, 1993



	R_1	R_1
pratioside A	H_2	OH
pratioside D_1	O	H
pratioside E_1		H
pratioside F_1		OH



pratioside B:
26-*O*-β-D-glucopyranosyl-22-hydroxy-(25R
)-furost-5-en-3β,17α,26-triol
3-*O*-β-D-glucopyranosyl-
(1→2)-β-D-glucopyranosyl(1→4)
β-D-galactopyranoside



pratioside C:
27-*O*-β-D-glucopyranosyl-isonarthogenin-3-
O-β-D-glucopyranosyl(1→2)-β-D-glucopyrano
syl(1→4) β-D-galactopyranoside

Table 3. Saccharides isolated from *Polygonatum* species

species	plant's part	saccharide	reference
P. sewerzowii	rhizome	seweran:manno- and glucopyranose moieties bound by β-1→4 linkage in a 15.4:1 ratio. arabinose, mannose, glucose, galactose.	Rakhimov *et al.*,1978
	rhizome	severan (a glucomannan): β-1→4 linked linear chain consisting of glucopyranose and mannnopyranose.	Rakhmanberdyeva *et al.*,1982; Rakhimov *et al.*, 1985
	stem	galactose	Rakhmanberdyeva *et al.*,1979
	rhizome,leaf	D-mannose	
	stem	glucofructan, fructose, glucose.	Rakhmanberdyeva *et al.*,1986a
	rhizome	psewerin (a glucofructan): a linear structure of 2→1 and 2→6 linked fructofuranose residues.	Rakhmanberdyeva *et al.*,1986b
	rhizome	psewerin (a glucofructan): nystose, sucrose, fructose, glucose	Rakhmanberdyeva *et al.*,1986a
P. roseum	rhizome	mannose, glucose, galactose, arabinose.	Arifhodzhaev *et al.*,1980
(Ledeb.) Kunth	rhizome	a glucomannan: a native acetylated linear polymer consisting of β-1→4-bonded β-D-gluco- and mannnopyranoses	Rakhmanberdyeva *et al.*,1986c
P. verticillatum	rhizome	glucose, galactose.	Shanker *et al.*,1970
(L.) All.	rhizome	sucrose, glucose, fructose	Srivastava *et al.*,1969
P. odoratum var.*japonicum*	rhizome	Polygonatum-fructan O-A: 29 units of fructose and 1 unit of glucose. Polygonatum-fructan O-B: 26 units of fructose and 1 unit of glucose. Polygonatum-fructan O-C: 18 units of fructose and 1 unit of glucose. Polygonatum-fructan O-D: 10 units of fructose and 1 unit of glucose.	Tomoda *et al.*, 1973
P. odoratum Druce var. *pluriflorum*	rhizome	D-fructose, D-mannose, D-glucose, D-galacturonic acid, which the ratio of them is 6:3:1:1.5.	Tomoda *et al.*,1971
P. odoratum Druce var. *pluriflorum*	rhizome	Oligosaccharide I: O-β-D-glucopyranosyl-(1→4)-D-mannopyranose. Oligosaccharide II: O-β-D-mannopyranosyl-(1→4)-D-mannopyranose. Oligosaccharide III: O-β-D-mannopyranosyl-(1→4)-D-glucopyranose. Oligosaccharide IV: O-β-D-mannopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→4)-D-mannopyranose. Oligosaccharide V: O-β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranosyl-(1→4)-D-mannopyranose. Oligosaccharide VI: O-β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranosyl-(1→4)-D-mannopyranose.	Tomoda *et al.*, 1973

Table 3 (cont 1). Saccharides isolated from *Polygonatum* species

species	plant's part	saccharide	reference
P. odoratum (Mill.) Druce	stem root	Rhamnose, Arabinose, Xylose, Galactose, Mannose, Glucose, Uronic acids	Tomschich *et al.*, 1996
P. stenophyllum Maxim.	stem root	Rhamnose, Arabinose, Galactose, Mannose, Glucose, Uronic acids	Tomschich *et al.*, 1996
P. glaberrimum C. Koch	rhizome	D-mannose, D-glucose and aetyl groups at a molar ratio of 8:1:3.5	Barbakadze *et al.*, 1993
P. falcatum A. Gray	rhizome	The six saccharides I,II,III,IV,V and VI are also isolated as above.	Tomoda *et al.*,1973
P. falcatum A. Gray	rhizome	falcatan (a polysaccharide): fructose, mannose, glucose, galacturonic acid.	Tomoda *et al.*, 1972
P. sibiricum Redoute	rhizome	polysaccharides A, B and C composed of glucose, mannose and galacturonic acid. oligosaccharides A, B and C composed of glucose and fructose.	Tao *et al.*, 1986
P. polyanthemum (M.B.] Die.	leaf, stem, rhizome, root	ramnose, arabinose, xylose, glucose, galactose	Rakhmanberdyeva *et al.*, 1982a
P. severzovii	rhizome	severan (a glucomannan): a linear chain of β-1→4-bound residues of D-glucopyranose and D-mannopyranose	Rakhmanberdyeva *et al.*, 1982b
P. orientale	rhizome	galactose, glucose, xylose	Yesilada *et al.*, 1991

Zanlanscianense Pamp. Dioscin had significantly the inhibitory effects on the growth of the human leukemia cell HL-60, inducing the differentiation and apoptosis. The HL-60 cells were induced mainly along the granulocytic lineage. Moreover, dioscin affects many cancer cells (Wang *et al.*, 2001).

From the ethanol extract of Chinese traditional medicine, rhizomes of *Polygonatum odoratum*, a new steroidal saponin POD-II together with β-sitosterol and its glucoside, and three known saponins were isolated. The structure of POD-II was elucidated as 3-O-β-D-glucopyranosyl-(1-->2)-[β-D-xylopyranosyl-(1-->3)]-β-D-glucopyranosyl-(1-->4)-galactopyranosyl-25(R)-spirost-5-en-3β,14α-diol. POD-II could induce the colony stimulating factor (CSF) in mouse serum. POD-III, at the low concentration, was shown to synergize the suboptimal and optimal concentration of Con A and lipopolysaccharide to stimulate lymphocytes proliferation (Lin *et al.*, 1994).

Polysaccharides

Generally, polysaccharides, lipids, nucleic acis (DNA) and proteins can be combined in the reactive antigens such as lipopolysaccharides, glycopeptides, nucleoproteins an other bioactive components. First, polysaccharides compose very commonly a part of more complex molecule which found the surface of human cells and also most animal cells. Second, polysaccharides are a major componets in the cell walls of plants and microorganisms. Lipids themselves could not become antigens. Interestingly, when these lipids are combined with other bioactive molecules such as polysaccharides to form the lipopolysaccharides (LPS), the lipids could change to antigens. Then, when the produced antigen entered our body, the normal healthy immune systems could be stimulated to enhance the immune responce. Two diverse properties of white blood cells such as macrophages, neutrophils eosinophils, basophils, and lymphocytes

sucha as helper or natural killer (NK) cells could response by phagocytosing and processing these antigens (Berjamini and Leskowski, 1988). An alcoholic extract of *Polygonatum odoratum* does not only had the increase of phagocytosis and the higher index of phagocytosis of macrophages, but also hemolysin and proliferation of lymphocytes up to normal level in mice with II+burn injury covering 5% body surface. This suggests that *Polygonatum odoratum* could apply as an immunopotentiator for a burn injury remedy to human (Xiao *et al*., 1990).

It has been found that some polysaccharides in *Polygonatum* species have the biological activities, such as their physiological actions which include anticoagulation, antidiarrheal and anticancer activities becuase of ability to raise the immunity levels of human. A protein-bound polysaccharide showed a blastoid transformation of human lymphocytes culture (Ohno *et al*., 1976). Saccharides isolated from *Polygonatum* species are mainly both polysaccharides and oligosaccharides as shown in Table 3 (Tomoda and Nakatsuka, 1972; Srivastava *et al*., 1969; Shanker *et al*., 1970; Tomoda *et al*., 1971; Tomoda *et al*., 1973a; Tomoda *et al*., 1973b; Rakhimov *et al*., 1978; Rakhmanberdyeva *et al*., 1979; Arifhodzhaev *et al*., 1980; Rakhmanberdyeva *et al*., 1982a; Rakhmanberdyeva *et al*., 1982b; Rakhimov *et al*., 1985; Rakhmanberdyeva *et al*., 1986a; Rakhmanberdyeva and Rakhimov, 1986c; Rakhmanberdyeva *et al*., 1986b; Tao Hong and Shang, 1986; Ono *et al*., 1988; Barbakadze *et al*., 1993; Tomshich *et al*., 1996).

The ability of depression on the release of a lambda (λ) phage lysogenic strain for *Polygonatum radix* was examined. *Polygonatum radix* was the strong depressors for the strain and also had an inhibitory effect on the SOS response in the SOS chromosome with a dose-effect response of the strains. More interestingly, *Polygonatum radix* decreased the frequency of the gene convention in Saccharomyces cerevisiae in the presence of hydroxyurea. Then, the purified component had an inhibitory effect on SOS response in *Escherichia coli* GW1060 (recA441), however, had no effect on the SOS network gene expression in *Escherichia coli* GW1107 (recA51). From these facts, *Polygonatum radix* might contain an inhibitor of the RecA protease (Wang *et al*., 1991).

The roots of *Polygonatum multiflorum* [L.] All. and *Polygonatum verticillatum* were found the two lectins. The both lectins contains the high content of asparaginic acid per the lectin. *Polygonatum verticillatum* contained around 28% asparaginic acid per the lectin. Two lectins agglutinated both the rabbit and rat erythrocytes, but did not agglutinate the human, cow, sheep and frogerythrocytes (Antoniuk, 1993). A carbohydrate-binding protein in rhizome of *Polygonatum multiflorum* was found as a Polygonatum lectin of the superfamily of a monocot mannose-binding lectin. Presumed carbohydrate-binding sites of the lectin can accomodate a mannose residue, whereas most of the carbohydrate-binding sites of the lectin-related protein cannot accompdate a mannose residue. By isolation and characterization of cDNA clones encoding *Polygonatum multiflorum* agglutinin (PMA) of a tetrameric lectin and a lectin-related protein, one member of the large family might lose its capacity to bind the carbohydrates (Damme *et al*., 1996). The leaves of *Polygonatum multiflorum* L. contain a mannose-binding lectin two galactose/*N*-acetylgalactosamine (Gal/GalNAc)-binding type 2 ribosome-inactivating proteins (RIPs). The both RIPs exhibit the similar RNA *N*-glycosidase activity each other, but differ in respect of both their specific agglutination activity and carbohydrate-binding specificity, PMRIPt being a GalNAc-specific lectin whereas PMRIPm is Gal/GalNAc-specific. The toxicity tests indicated that both *Polygonatum* RIPs showed a very low cytotoxicity against the human and animal cells. The genomic clones encoding both RIPs revealed a high degree of sequence similarity to other type 2 RIPs. From analysis of molecular modelling, two *Polygonatum* RIPs have a similar structure to ricin (Van *et al*., 2000). The most prominent protein of *Polygonatum multiflorum* rhizomes was found as a mannose-binding lectin, which belongs to the superfamily of monocot mannose-binding proteins. A screening of cDNA libraries constructed with RNA isolated from buds, leaves and flowers of *P. multiflorum* also yielded the cDNA clones encoding a protein, which contains two tandemly arranged domains with an obvious sequence homology to the mannose-binding lectins (Van *et al*., 1996).

Miscellaneous compounds Further, other compounds have been found from certain *Polygonatum* species.

For example, alkaloids were isolated from *P. biflorum* (Walt.) Ell. (Crum *et al*., 1965) and C25 - C32 aldehydes from the leaves of *P. odoratum* (Mill.) Druce (Isono *et al*., 1974). Allantoin, which is produced by the oxidation of uric acid, widely distributed in nature such as urine of animals, seeds and roots of plants, and generally has a stimulating activity for the epithelical formation as a skin ulcer therapy, has been isolated from *P. officinale* All., *P. latifolium* [Jacq.] Desf., *P. verticillatum* [L.] All., and *P. multiflotum* [L.] All., (Constantinescu *et al*., 1969). β-Sitosterol with anticholesteremic activity was isolated from the rhizome of ten *Polygonatum* species (*P. stenophyllum* Maxim (Glebko *et al*., 1985), *P. verticillatum* [L.] All. (Srivastava *et al*., 1969), *P. officinale* All. (Okanishi *et al*., 1975), *P. odoratum* (Mill.) Druce, *P. humile* Fisch. ex Maxim., *P. inflatum* Kom., maximowiczii Fr. Schmidt, *P. acuminatifolium* Kom., *P. involucratum* (Franch. et Savat.) Maxim., and *P. desoulavyi* Kom. (Glebko *et al*., 1988), and polygonaquinone was isolated from the rhizome of *P. falcatum* A. Gray, which has been widely as a folklore medicine in eastern Asia although its physiological action is unclear (Nakata *et al*., 1964).

CONCLUSIONS

In this review, three main classes of chemical compounds have been shown in *Polygonatum* species which have certain specific functional activities. The Directory (Jiangsu New Medical College, 1977 g) shows that the applications of medicine of *Polygonatum* species are very common especially in China as Chinese traditional medicines and the applications and the treatments for the different diseases have a long history of use as a medicine for their restorative powers. They are also found in the use in parts of eastern Europe, Japan and southern Asia. On the other hand, recently, a combination therapy of modern Western medicine with Chinese medicine have begun to try for the better treatments of curing and preventing the diseases. The chemical constituents in *Polygonatum* species are clearly established. Because of these long, historical uses of *Polygonatum* species by their different cultures (e.g. Japan and China) for medicinal purposes, more newly functional active components should be warranted in the future.

ACKNOWLEDGEMENTS

This study was supported in part by a Grant from the Apparatus Fund 2002 of Josai University.

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